Minireview

Split-Liver Transplantation: A Review

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Split-liver transplantation (SLT), a procedure where one cadaver liver is divided to provide for two recipients, offers immediate expansion of the existing cadaver donor pool. To date, the principal beneficiaries of SLT have been adult/pediatric recipient pairs with excellent outcomes reported; however, the current scarcity of cadaver organs has renewed interest in expanding these techniques to include two adult recipients from one adult cadaver donor. Significant obstacles to the widespread application of SLT exist and must be resolved by the transplant community before greater utilization can be realized. This manuscript reviews the historic background, surgical techniques, current results, and obstacles impeding further application of SLT.

Key words: Hepatobiliary surgery, liver transplantation, organ donation, partial-organ liver transplantation, pediatric liver transplantation, split-liver transplantation

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Historic Background

Transplantation of partial-liver allografts was initially advocated by Smith, who proposed the left lateral segment as suitable for children in 1969 (1). Smith’s proposal remained untested until the 1980s, when increasing demand for pediatric cadaver organs resulted in prolonged waiting times and increased wait-list mortality (2,3). Initial attempts to create pediatric partial-liver allografts focused upon the surgical reduction of a larger child or adult cadaver organ to fit the abdominal cavity of the recipient, termed reduced-liver transplantation (RLT), which was simultaneously reported by Bismuth (4) and Broelsch (5) in 1984. Early efforts were plagued by technical difficulties; however, later series demonstrated RLT graft outcomes equaled or exceeded cadaver whole-organs in children (6–8). While improved outcomes had been achieved in the treatment of children, the discard of a right hemi-liver and the increased competition created between adult and pediatric candidates for the same donor pool rendered the procedure impractical (2,9,10).

To expand the donor pool, the surgical techniques of RLT were modified to create a pediatric left lateral segment graft with a remnant graft suitable for transplantation of an adult. These techniques could be applied to cadaver donors in the performance of SLT (11,12) or to live volunteers to create living-donor liver transplantation (13,14).

Pichlmayr (11) and Bismuth (12) each reported successful split-liver transplantation in 1989. Emond from the University of Chicago reported an initial series of nine SLT procedures in 18 adult and pediatric recipients in 1990 (15). Overall patient and graft survival were lower than whole-organ recipients with a higher incidence of complications and need for re-transplantation (15). While the outcomes were inferior to cadaver whole-liver transplantation, the early data were promising, leading the authors to conclude ‘[SLT] is feasible and could substantially impact transplant practice’ (15). Interest in SLT precipitously declined when an expanded University of Chicago series failed to demonstrate improved SLT outcomes vs. cadaver whole-organs or partial-organ allografts from living donors (16).

Select European centers pursued SLT with de Ville de Goyet reporting data on 100 grafts from the European Split Liver Registry in 1995 (17). Recipient and graft survival correlated to medical acuity at transplantation with elective pediatric recipient and graft survival of 89% and 80%, respectively. In the setting of urgent medical acuity, recipient and graft 6-month survival were only 61%. Elective adult recipient and graft survival were 80% and 72%, vs. 67% and 55%, respectively, for adults requiring urgent transplantation. Twenty percent of grafts were lost to complications including hepatic artery thrombosis (11%), portal vein thrombosis (4%), and a 19% incidence of biliary complications (17). These data were significantly improved from previous SLT series and equivalent to European Liver Transplant Registry survival data for cadaver whole-organs.

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technical manipulation. Broelsch (18) and Busuttil (19) introduced a technique to perform the split-piece in situ at the donor hospital with surgical division completed in the heart-beating cadaver immediately prior to aortic cross clamp and organ cold perfusion.

In situ SLT requires specialized skills and prolonged operating room time at the donor institution. Increased logistics coordination is necessary, but SLT can routinely be performed without special equipment or impedance of thoracic or additional abdominal organ procurements (20,21). In situ separation reduces cold ischemia, simplifies identification of biliary and vascular structures (18,22), eliminates unintentional graft re-warming during ex vivo manipulation, and reduces hemorrhage upon graft reperfusion (22,23). Preliminary in situ SLT data from the University of Hamburg in 1996 (24) and the University of California Los Angeles (UCLA) in 1997 (19) yielded pediatric as well as adult recipient graft and patient survival that equaled or exceeded whole cadaver-organ data.

Since their initial reports, both UCLA (25) and the University of Hamburg (26) have published expanded series confirming previous outcomes. UCLA has the largest in situ SLT experience with more than 100 procedures performed and has adopted the in situ technique as routine when an optimal donor is available (27). With this commitment, SLT accounts for approximately 10% of adult and 40% of pediatric grafts at UCLA (27), but only 2% of all transplants performed nationally over the past decade (28). Split-liver transplantation and living donation are complementary, not competitive, strategies for expansion of the donor pool; however, as SLT preserves the benefits of pediatric living-donor liver transplantation without incurring donor risk (20,27,29), it is the authors’ procedure of choice.

Surgical Techniques

Donor selection
Paramount to the success of SLT is donor and recipient selection. We (27) and others (22,30) have restricted donor selection to optimal candidates with respect to age, ABO compatibility, size-match, liver function, vasopressor requirements, absent/scant arrest period, brief donor hospitalization, and serum sodium concentration. These donor criteria have not been assessed prospectively and may be unnecessarily conservative; however, SLT involves an element of risk and the consequences of primary nonfunction in two patients at the same time are devastating. Accurate donor assessment from the recovery team is equally important. Potential grafts must be assessed for size, vascular and biliary anatomy, as well as parenchyma quality and quantity.

Split-liver transplantation requires extended dissection either within the heart-beating donor or on the back table ex vivo. The increased blood loss and volume replacement incurred during in situ SLT has prompted concerns that the quality of thoracic organs may be affected (31). Data from our center on 100 consecutive in situ procedures and others with a commitment to in situ SLT suggest the effect on additional abdominal and thoracic organs is negligible (21) (27). We allocate 90 min of additional operating room time for an adult/pediatric in situ SLT and 3 h for an adult/adult in situ SLT. While longer procurement times have been reported (30), in situ SLT has not been an excessive temporal burden in our experience, provided adequate communication has occurred between all procurement teams (27). We routinely advise the organ procurement agency of a potential in situ SLT at the time of offer so other procurement teams can adjust their arrival schedules. Unfortunately, no data exists on the additional costs incurred by the performance of in situ SLT.

Anatomic principles
Any technical description must begin with the anatomic classification system of Couinaud (32) refined by Bismuth (33) (Figure 1), which has been universally accepted by the transplant communities of Europe, Asia, and North America as the reference for describing partial-organ allografts. The liver is divided into eight functional units, termed 'segments', that receive separate hilar pedicles: each containing a portal venous branch, hepatic arterial branch, and a hepatic venous branch (dark blue) and separated by connective tissue scissurae. Reprinted from Liver Transplantation, Vol. 7(12); 2001: 1077–1080, with permission from the American Association for the Study of Liver Diseases.

Figure 1: Segmental liver anatomy. The segmental anatomy of the liver as described by Couinaud (32) and Bismuth (33). Each anatomic segment (roman numeral) receives a unique portal pedicle (light blue) consisting of a portal venous branch, hepatic arterial inflow, and bile duct. Individual segments are drained by unique hepatic venous outflow branches (dark blue) and separated by connective tissue scissurae.
Surgical division of the liver along the middle hepatic vein (yellow line labeled ‘A’) yields a left lobe (segments I–IV) and right lobe (segments V–VIII) graft that can be utilized in SLT between two adults. Division along the falciform ligament (white line labeled ‘B’) yields the pediatric left lateral segment graft (segments II–III) and the remnant, adult right trisegment graft (segments I, IV–VIII).

Hepatic parenchyma transection corresponds to ‘scissurae’ or connective tissue planes that separate individual liver segments, thereby reducing intraoperative blood loss and postresection parenchyma ischemia. Couinaud’s classification permits the creation of functionally distinct partial-organ allografts (Figure 2). Division of the hepatic parenchyma at the falciform ligament yields a segment II/III graft, termed a left lateral segment graft, of approximately 250cc in volume for pediatric recipients (27) (34), and a remnant Couinaud segment I, IV–VIII ‘right trisegment’ graft of approximately 1100cc for transplantation of adults (27). The left lateral segment graft can be further reduced to a ‘monosegment graft’ (segment III) for very small infants and neonates (Figure 3; 35).

For transplantation of two larger individuals from one adult cadaver donor, the liver can be divided along the middle hepatic vein to create two nearly equal-sized grafts (Figure 2). Left lobe grafts of approximately 400cc in volume can be created with (segments I–IV) or without the caudate lobe (segments II–IV) for recipients with typically less than 60 kg of body mass. Right lobe grafts (segments I, V–VIII, or V–VIII) have a typical volume of approximately 800–1000cc and are generally suitable for candidates ≤80 kg (36–39).

Creation of left lateral segment II, III and right trisegment I, IV–VIII grafts
Prior to the performance of any split procedure, the standard techniques of abdominal organ procurement, including supra-celiac and infra-renal aortic dissection as well as cannulation of the inferior mesenteric vein, should be completed to insure that if a donor were to become unstable, the SLT could be aborted with rapid progression to aortic cannulation, cross-clamp, and organ cold perfusion (40).

Split-liver transplantation is initiated with division of the falciform ligament to expose the hepatic vein-caval junction. The left hepatic vein is isolated and encircled with a vessel loop. Occasionally, the division of the middle and left hepatic veins will not be distinguishable or segments II and III will have independent orifices to the cava (41). A common middle and left hepatic vein requires separation after parenchyma division. Recognition of independent segment II and III veins is critical to avoid inadvertent injury and requires that both orifices are incorporated on a common caval patch (41).

Hilar dissection begins at the base of the round ligament with isolation of the left hepatic artery, left portal vein branch, and left bile duct branch. The left hepatic artery is encircled and dissection is continued along its entire length. Particular attention is devoted to the preservation of segment IV penetrating arteries (41,42) (Figure 4). If the segment IV branch arises high off the left hepatic artery and provides significant inflow, our practice is to anastomose the segment IV artery to the right trisegment graft’s gastro-duodenal remnant. Portal venous branches to segment IV are ligated and divided lateral to the umbilical fissure to isolate the entire left portal vein.

With vascular control of the left lateral segment achieved, parenchyma transection is initiated with electrocautery by scoring the liver surface approximately 1 cm to the right of the falciform ligament (41). The parenchyma is divided...
between the left lateral segment and segment IV and carried to 1 cm above the left bile duct in the umbilical fissure (42). Small penetrating vessels and biliary radicles are suture ligated as required. The left hilar plate, containing the bile duct, is sharply transected. This separates the left lateral segment from the remaining parenchyma with its own vascular pedicle and venous drainage. Following cold perfusion, the left hepatic artery, the left portal vein, and the left hepatic vein are sharply divided and the left bile duct flushed with cold University of Wisconsin (UW) solution® (Viaspan, Pomona, NY) prior to storage (Figure 5). The right trisegment graft is removed in the standard fashion and stored at 4°C in UW solution (40).

Transplantation of the left lateral segment graft requires preservation of recipient inferior vena cava. The right hepatic vein orifice to the vena cava is suture ligated, as are the smaller accessory hepatic veins along the inferior vena cava. The left and middle hepatic vein orifices are opened to form a large common trunk for hepatic venous anastomosis (43). All anastomoses are performed with surgical telescopes of between ×2.5 and 4.5. Anastomosis of the portal vein is performed end-to-end utilizing nonabsorbable monofilament suture. For infants and neonates, the anastomosis is run on the posterior wall and interrupted anteriorly. The donor hepatic artery is anastomosed to the recipient common hepatic artery or to the infrarenal aorta by a cadaver artery interposition graft utilizing interrupted ≥7–0 nonabsorbable monofilament suture. Biliary anastomoses are occasionally performed duct-to-duct, but more frequently are performed by end-to-side hepato-jejunostomy using a single-layer, interrupted 6-0 absorbable suture with an internal stent.

Preparation of the right trisegment graft for transplantation includes removal of remnant diaphragm from the liver bare area, ligature of phrenic vein origins, closure of the left hepatic vein, left portal vein, and left hepatic artery organs with possible re-vascularization of a segment IV arterial branch, and oversew of the left bile duct remnant. The parenchyma surface is carefully inspected during back-table preparation for possible vascular and biliary leaks that are oversewn. Gently flushing each structure aids in the identification. The graft is now ready for transplantation, utilizing standard whole-organ techniques (40).

Creation of left segment II, III, IV and right segment I, V–VIII grafts

Grafting of left lobe segments II–IV is applicable to toddlers, teenagers, and adults less than 80 kg in weight (37). The dissection proceeds in a similar fashion as above to identify the hepatic vein origins. In this technique, the middle and left hepatic veins are together encircled with a vessel loop to guide parenchyma dissection. The left bile duct, left hepatic artery, and left portal vein (42,44) are identified with dissection carried distal along the entire extra-hepatic length to the level of the round ligament. Left hepatic artery branches servicing segment IV are preserved (Figure 4). The left portal vein is freed along its entire length with division of all caudate lobe branches.

Occlusion of the left portal vein and left hepatic artery generates a demarcation plane for parenchyma transection. The plane is marked by electrocautery and proceeds to the hilar plate, ligating parenchyma vessels as encountered. At the hilar plate, the left bile duct is sharply transected. The left hepatic artery and left portal vein are preserved for organ cold perfusion. Heparin is administered followed by aortic cannulation, cross-clamp, and organ cold perfusion. Split-liver transplantation continues with sharp transection of the left portal vein just distal to the bifurcation and transection of the right hepatic artery just distal to its takeoff from the proper hepatic artery. The common portal vein...
Figure 6: Arterial supply of segment IV from the right hepatic artery. The hepatic corrosion casts depict >1-mm branches of the right hepatic artery crossing Cantlie's line to supply segment IV. (A) Right hepatic artery (RHA) branch to segment IV (crossing branch) is superior and posterior to the portal bifurcation (PV: portal vein, LPV: left portal vein, RPV: right portal vein, LHA: left hepatic artery, PHA: proper hepatic artery). (B) Right hepatic arterial branch to segment IV (crossing branch) is anterior to the left portal vein. Reprinted from Liver Transplantation, Vol. 7(12); 2001: 1077–1080, with permission from the American Association for the Study of Liver Diseases.

Recognition of the significance of middle hepatic venous branches in the drainage of segments V and VIII (45–47) (Figure 8) have led our team to include these branches in vena cava anastomoses, which may require vascular conduit.

Creation of left segment I–IV and right segment V–VIII grafts

Left lobe grafts (segments I–IV) that include the caudate lobe may be used for adults weighing as much as 65 kg and, in select circumstances, heavier individuals (38,39). Segment V–VIII grafts generally permit size-for-size donor to recipient weight ratios or even slightly smaller donors to donate to larger recipients. As described earlier, the hepatic veins are identified and the right hepatic vein is encircled with a vessel loop. The diaphragmatic attachments to the liver are released with the dissection continued on the right lobe to the inferior vena cava. The left border of the inferior vena cava is not disturbed. Accessory hepatic veins are encountered in approximately 15% of cadaver donors and are
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Figure 8: Middle hepatic vein (MHV) draining segments V and VIII. (A) Corrosion cast demonstrating a dominant MHV which sweeps laterally to drain segments V and VIII. Three large communicating branches (lettered A, B, C) create a collateral flow within segments V and VIII between the middle and right hepatic vein (RHV). (B) This anatomic variant is further depicted during intraoperative ultrasound. Reprinted from Liver Transplantation, Vol. 6(3); 2000: 367–369, with permission from the American Association for the Study of Liver Diseases.

Following retrograde cholecystectomy, the hepatoduodenal ligament is opened to expose the hilum. The right hepatic artery is identified and exposed lateral to the common hepatic duct. Of note, the right hepatic artery is rarely anterior to the common hepatic duct except in the circumstance of replaced arterial anatomy. Lateral exposure avoids skeletonization of the proper hepatic bifurcation thereby preserving arterial supply to segment IV from the right hepatic artery (Figure 6). The right portal vein is approached from the right side of the hilum (lateral) and dissected to the level of the bifurcation where it is encircled with a vessel loop (Figure 9). A Pringle maneuver of the left hilum is performed to create a demarcation line for parenchyma division. The left bile duct is sharply divided at the hilar plate and bleeding points secured with 6:0 nonabsorbable monofilament suture. Parenchyma division is performed along the main portal fissure with the surgeon’s left fingertips positioned behind the right lobe anterior to the inferior vena cava. Segment V and VIII venous tributaries are sharply divided for later revascularization. Upon completion of parenchyma division, the right hepatic vein, right portal vein, and right hepatic artery are maintained for organ cold perfusion (Figure 10). Graft separation includes sharp division of the right portal vein just distal to the bifurcation and transection of the right hepatic artery just distal to its takeoff from the proper hepatic artery. The right hepatic vein is divided from the suprahepatic vena cava as a patch and the right segment V–VIII graft is removed. The bile duct is flushed prior to cold storage in UW solution. Ex vivo preparation of the segment V–VIII graft includes suture ligation of small biliary radicles and potential restoration of segment V and VIII venous outflow (Figure 8).

The left segment I–IV graft is removed, utilizing standard organ recovery techniques followed by irrigation of the common bile duct and storage in cold UW solution (40). Ex vivo preparation includes closure of the right portal vein orifice, right hepatic vein orifice, and right hepatic artery orifice, as well as suture ligation of parenchymal biliary radicles.

Right lobe segment V–VIII grafts require the recipient’s inferior vena cava (40). The graft is positioned orthotopically with a graft hepatic vein to recipient right hepatic vein orifice anastomosis or to a common trunk formed by the recipient’s remnant left, middle, and right hepatic vein orifices (30,38). Middle hepatic venous branches are individually preserved with a caval patch for implantation if larger than 5 mm in diameter.
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Figure 10: Completion of parenchymal transection. The parenchymal dissection has been completed and the grafts are ready for cold perfusion. The left bile duct has been separated; however, the hepatic arterial (left hepatic artery encircled by red vessel loop) and portal venous systems are intact.

draining segments V and VIII (45–47) (Figure 8) as well as accessory hepatic veins ≥5 mm in diameter are included in anastomoses either directly to the vena cava or through utilization of venous conduit. End-to-end anastomosis of the portal vein is frequently possible, as is the right hepatic artery to a suitable inflow source from the common hepatic artery. Donor iliac artery or vein may be used for interposition grafting. Biliary drainage may be achieved through end-to-end anastomosis or Roux-en-Y hepaticojejunostomy.

Technical considerations
All techniques described require only standard surgical facilities with no specialized equipment and have been performed concomitant with additional abdominal and thoracic organ procurements. Surgical anatomy is defined during the donor procedure, particularly if parenchyma division is performed in situ, as preoperative liver imaging is not practical in most donor hospitals. In ex vivo SLT, dissection may be augmented by cholangiography as well as angiography.

Successful SLT requires recognition that partial-liver grafts predispose to unique complications resulting from anatomic variations as well as recipient physiology. Technical challenges include the creation of sufficient liver volume to meet the metabolic demands of the recipient, graft positioning to optimize vascular flow and biliary drainage, as well as an appreciation of anatomic variations that necessitates complex biliary or vascular reconstruction. Frequent complications among SLT recipients include parenchymal bile leak, hepatic arterial thrombosis, hepatic venous outflow obstruction, infection from remnant necrotic tissue, and poor graft function secondary to insufficient hepatic volume. Graft mass is a critical variable affecting outcomes and a limitation in the extension of SLT between two adults. Adequate graft mass has been extensively explored in living donor liver transplantation with minimal graft thresholds advocated (48–52); however, these data are not directly applicable to SLT as parenchyma quality, and immediate function of living donor grafts exceeds that of cadavers (27,53,54). Our preference is a graft mass of at least 1% recipient body weight; however, grafts less than 0.8% recipient body weight have been utilized with success (30,55,56).

Inadequate graft mass for the recipient manifests as a pattern of dysfunction associated with portal hyperperfusion, prolonged cholestasis and gradual recovery, termed ‘small-for-size syndrome’ (48,55). ‘Small-for-size syndrome’ is characterized by synthetic dysfunction, a mild transaminisits (×2–4 upper limit of normal), and prolonged cholestasis. Improved synthetic function typically occurs within 72 h of reperfusion as the graft undergoes rapid hypertrophy. Cholestasis improves gradually over a course of weeks. Stable synthetic function signals a reversible situation that will improve as the graft undergoes regeneration; however, the appearance of, or inability to, reverse encephalopathy, hypoglycemia, metabolic acidosis, or augmentation of synthetic function beyond 48 h heralds irreversible graft failure that should prompt re-transplantation. Graft biopsy reveals a pattern of diffuse ischemic injury demonstrating hepatocyte ballooning, steatosis, centrilobular necrosis, and parenchymal cholestasis that may be misinterpreted as preservation injury (48). Pathologic changes frequently subside within 2 weeks of transplantation, except for the presence of cholestasis that may persist for weeks. While radiologic data demonstrate the majority of volume regeneration occurring within 7 days after living-donor liver transplantation (57,58), small-for-size grafts should be considered highly vulnerable during the immediate postoperative period to insult with an increased risk of developing sequelae from complications or additional metabolic stress.

Current Results
The absence of a dedicated SLT registry has limited data to individual center reports. An abstract from the Joint Meeting of the International Liver Transplantation Society, European Liver Transplantation Association, and the Liver Intensive Care Group of Europe in 2001 suggested that...
split procedures represented 3.7% of the total grafts from the European Liver Transplant Registry between May 1968 and June 2000 (59); however, outcomes were not reported. The American Society of Transplant Surgeons (ASTS) has recently performed a survey of 89 North American transplant centers participating in the United Network for Organ Sharing (UNOS) Scientific Registry for Transplant Recipients (SRTR) on the utilization of SLT (28,60). This review summarizes outcomes from the ASTS survey, individual center reports, and SLT data from the SRTR.

The ASTS survey, performed between 04/00 and 05/01, elicited a response from 83 of 89 surgical teams identified from the Annual Report of the SRTR (61) as having performed at least one liver transplant procedure during the previous year. Thirty-six of the responding teams reported data on 207 left lateral segment, 152 right trisegment, 15 left lobe, and 13 right lobe grafts (60). Split-liver transplantation was most frequent in the setting of at least one urgent recipient with the majority of each graft type applied to UNOS status I and IIA recipients. Five groups reported sharing 18 grafts over a distance of <10 miles to across the United States. Experience was concentrated among 13 groups reporting five or more SLT procedures that accounted for 221 grafts or 57% of the cumulative data. The majority of groups reporting experience with SLT (63%) had performed less than five procedures. Cadaver whole-liver transplantation volume correlated with the application of SLT (60).

Complications were frequent in all graft types with biliary and vascular complications equally distributed between grafts split by either ex vivo or in situ techniques. Primary nonfunction, graft failure, and recipient death correlated with recipient UNOS status at transplantation (60). The overall incidence of complications among left lateral segment recipients was 32% and relatively uniform across UNOS recipient status. However, the relative contribution of the complication type varied, with vascular complications being more frequent in critically ill recipients and biliary complications being more common among nonurgent recipients. Primary nonfunction and graft failure occurred principally in UNOS status I recipients. Recipient mortality was 4-fold more frequent in UNOS status I recipients with two-thirds attributed to graft-related complications (60).

While the majority of right trisegment grafts were utilized in nonurgent recipients, morbidity and mortality were concentrated among urgent, UNOS status I and IIA SLT recipients. The overall incidence of right trisegment graft complications was 26%, with biliary complications being most frequent, followed by vascular complications, and post-transplant hemorrhage. Hepatic artery thrombosis was the most frequently reported vascular complication with five reported cases of hepatic artery pseudoaneurysm and one hepatic artery disruption. There was a 4% incidence of primary nonfunction and a 15% incidence of mortality with more than one-half of deaths being attributed to graft-related complications (60).

Single-center outcomes for the performance of adult/pediatric SLT are summarized in Table 1. The 32% incidence of left lateral segment graft complications reported by the ASTS survey is similar to data from individual centers, as is the classification of complications.

Table 1: Adult/pediatric split-liver transplantation

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<th>Center</th>
<th>Author</th>
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<th>Recipient</th>
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<td>1996</td>
<td>7</td>
<td>100%</td>
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n = graft number, recipient = recipient survival, graft = graft survival, comp = reported overall complication rate, N/A = data not reported.
with biliary complications being most common (29), followed by a 5–9% incidence of vascular complications (29,62,63). Right trisegment graft data were also similar between the ASTS survey and the single-center reports with respect to the incidence and nature of complications (Table 1). All studies identify poor outcomes in the setting of urgent SLT (27).

Sparse data exist on SLT between two adults, as these techniques have been cautiously implemented among select transplant centers. Left and right lobe graft data from the ASTS survey do not permit meaningful analysis. The reported overall incidence of left lobe complications was 26% vs. 22% for right lobe grafts, with the majority utilized for urgent recipients (60). Biliary complications were most frequent with vascular complications reported in 4% of left lobe vs. 9% of right lobe grafts. Primary nonfunction and graft failure were 7% and 9% for left lobe vs. 9% and 14% for right lobe grafts, respectively. Recipient death was observed in 7% of left vs. 8% of right lobe grafts.

Individual center data on adult/adult SLT are summarized in Table 2. The Paul Brousse group has reported the largest series on adult/adult SLT (22,56,64). In 1996, Bismuth reported 1-year patient and graft survival of 79% and 78%, respectively, on 27 SLT grafts, with the routine application of ex vivo SLT increasing overall graft availability at their center by 28% (22). The incidence of biliary complications was 22% with a 15% incidence of arterial complications and one reported primary nonfunction. A later series comparing 1- and 2-year SLT patient and graft survival to adults receiving cadaver whole-organ transplantation over the same time period demonstrated right- and left-SLT graft 1-year recipient survival of 74% vs. 88%, respectively, with 1-year graft survival of 74% for right-SLT vs. 75% for left-SLT recipients (56). Graft complications were not uniformly distributed with a significantly higher incidence of biliary complications observed in left grafts and a higher incidence of arterial complications reported in right grafts (56). While no significant difference between whole-organ and SLT recipient 1-year survival was identified, the increased incidence of complications observed in SLT grafts contributed to a significantly decreased incidence of graft survival at 1-year, particularly among left-SLT recipients. The authors performed SLT in 15% of available donors and reported a 62% net increase in adult recipients through the routine application of SLT. They concluded that SLT between two adults can yield good outcomes; provided recognition of donor and recipient limitations as well as surveillance for complications unique to the procedure (66).

The University of Minnesota has reported the largest North American center data on adult/adult SLT. In 2001, Humar reported on 12 SLT grafts with patient and graft survival of 83% at a mean follow up of 9 months (30). Right lobe graft mean recipient weight was 89 kg vs. a mean weight of 60 kg for left lobe recipients. Ten of the 12 recipients, all of whom were nonurgent status at SLT, were alive and well. A later abstract by the same group reported nine procedures yielding 18 grafts with a mean follow up of 18 months (65). Seventeen of the 18 recipients were UNOS status IIB and one was UNOS status IIA. Patient and graft survival were 89% for right lobe vs. 78% for left lobe grafts. Biliary complications were most frequent (27%), followed by an 11% incidence of vascular complications that resulted in two deaths. There was one primary nonfunction in an unspecified graft.

Split-liver transplantation has been performed in Asia with organ sharing among countries (66,67). The total number of SLT procedures is low secondary to scarce cadaver donation, logistic, cultural, and manpower constraints; however, de Ville de Goyet has reported data on 26 grafts obtained by five Asian centers. Complications were not stratified by graft type but included parenchymal bile leak, portal vein thrombosis, portal vein stenosis, hepatic artery insufficiency, and T-tube dislodgement requiring celiotomy. Four deaths were reported, yielding an 85% overall recipient survival with at least one additional recipient requiring re-transplantation (67).

The above data (Table 2) are in general agreement with the ASTS survey data. Similar patterns of complications emerged from the ASTS survey data and the Paris group, with vascular complications being more frequent in right lobe grafts and biliary complications more frequent in left lobe grafts (56). Graft survival is higher in right lobe SLT recipients with a similar incidence of primary nonfunction and recipient death in each group (60).

Preliminary data from the UNOS SRTR has also become available on SLT. A data request from the Organ Procurement and Transplant Network Liver and Intestinal Transplantation Committee (68) was submitted to provide outcomes of SLT right lobe grafts in adults. As graft-specific coding does not exist in the database, a data search was performed for grafts classified as ‘partial right liver segments’ that had corresponding liver segments also transplanted or right ‘split liver segments’ prepared either ex vivo or in situ. Assuming SLT is restricted to optimal donors, partial right graft outcomes were compared with

<table>
<thead>
<tr>
<th>Center</th>
<th>Author</th>
<th>Year</th>
<th>n</th>
<th>Recipient</th>
<th>Graft</th>
<th>Comp</th>
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<tbody>
<tr>
<td>Minneapolis (65)</td>
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<tr>
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<td>83%</td>
<td>58%</td>
</tr>
<tr>
<td>Hamburg (26)</td>
<td>Broering</td>
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<tr>
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<tr>
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<td>Villejuif (22)</td>
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<td>1996</td>
<td>27</td>
<td>79%</td>
<td>78%</td>
<td>37%</td>
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n = graft number, recipient = recipient survival, graft = graft survival, comp = reported overall complication rate, N/A = data not reported.
two groups: a comparable group of whole-organ cadaver donors between 18 and 40 years of age, and a surrogate ‘marginal donor’ group consisting of cadaver whole-organ donors greater than 60 years of age. Between 1994 and 2001, 215 SLT right grafts were identified. These included 33 partial, 42 in situ, and 140 ex vivo grafts that were compared with 2901 grafts procured in donors >60 years old and 9802 grafts procured from donors aged 18–40 years (68). Outcomes, measured by graft failure and recipient death were stratified by medical urgency status and adjusted for body mass index, year of transplant, cause of death, ABO blood compatibility, history of previous liver transplant, indication for transplantation, cold ischemic time, creatinine >2 mg/dL, medical condition, and donor/recipient age, gender, and ethnicity. Graft failure and death occurred in 32% and 26% of right SLT recipients, respectively, with outcomes comparable to whole-organ grafts from donors >60 years of age, and inferior to outcomes from cadaver whole-organ donors aged 18–40 years. Split-liver transplantation grafts demonstrated a significantly increased relative risk of graft failure and death vs. cadaver donors aged 18–40 years (68). When stratified by recipient status, UNOS status I SLT recipients also demonstrated a significantly increased risk of graft failure and death vs. cadaver whole-organ donors aged 18–40 years. Significantly increased graft failure of SLT recipients vs. cadaver donors aged 18–40 years was observed in UNOS status IIB and III as well, but did not translate into significantly increased deaths (68). Split-liver transplantation graft data were comparable to the ‘marginal donor’ group with overall graft failure and death not being statistically different. Thus, the splitting of presumptive optimal donors yielded right SLT grafts that behaved similar to cadaver whole-organs procured from ‘marginal donors’ (68).

Comparison of in situ, and ex vivo SLT procurement techniques have not identified a distinct advantage. Morbidity and mortality was comparable between procurement methods, except for the incidence of postoperative hemorrhage, which was higher among ex vivo SLT recipients in the ASTS survey (60). Data from left lateral segment grafts suggest a higher incidence of primary nonfunction among grafts prepared ex vivo vs. in situ or living-donor (18,20,22–24,69); however, other transplantation centers have reported excellent results performing the ex vivo technique (22,56,64,70). The authors advocate the in situ technique prevents inadvertent graft re-warming, simplifies identification of vascular and biliary structures, and facilitates graft sharing by permitting direct graft shipment from the donor site without additional ex vivo separation.

Obstacles Impeding Further Utilization of SLT

The success of SLT applied to adult/pediatric pairs in the present climate of organ scarcity has fueled initiatives to expand efforts to include two adult recipients from one adult cadaver donor. However, substantial obstacles must be overcome prior to the further application of SLT. These obstacles include technical advancement, logistic, organ allocation, as well as issues of informed consent. As detailed earlier, SLT requires substantial planning and a superior surgical technique. To date, most SLTs have been performed in large centers that can support at least two concurrent recipient operations with experienced surgical teams. Technical considerations complicating SLT are still in evolution and must be further disseminated throughout the surgical community prior to any appreciable increase above current activity (71).

Split-liver transplantation requires substantial coordination once a suitable donor is identified. Recipient selection is principally limited by available left lobe or left lateral segment mass. Thus, to implement SLT between two adults, the team contemplating the procedure must have access to a diversity of recipients of different sizes that can be paired. This flexibility may require that centers collaborate to benefit the overall donor pool and compromise on individual access for global benefit. In Europe, where cadaver organs are allocated to centers, rather than specific patients, increased flexibility is available for recipient selection and coordination (71). The result has been standing agreements between centers for sharing of partial grafts that have been quite successful (31,72). The past UNOS policy permitting the unrestricted use of remnant grafts by the SLT center was a direct incentive for the application of SLT; however, in regions where multiple centers are competing for each donor, rigid allocation policies impede SLT application.

While we have utilized split-grafts for the treatment of UNOS status I recipients, we have avoided utilization of split-grafts in patients with advanced chronic liver disease requiring intensive care unit hospitalization (UNOS status IIA) (27). Disappointing results in decompensated cirrhotics with living donor and SLT grafts have made it apparent that critically ill patients fare poorly from these complex technical variants (27); although, previously well patients with fulminant hepatic failure may prove an exception. Complications are more frequent and poorly tolerated by the decompensated cirrhotic. Ironically, these are the patients to whom livers are preferentially allocated under the patient-driven system in the United States (71).

Requirements for consent with respect to SLT have not been defined. In contrast to the extensive ethical analyses that preceded living donor liver transplantation (73), relatively little discussion of the ethics surrounding SLT has occurred. As increased risk is inherent in the performance of SLT, it is customary to obtain specific informed consent for the procedure. Traditionally, patients have not been involved in the selection of cadaver donors; but the extended use of ‘marginal’ donors has brought the issue of consent to the forefront. The parameters governing these issues have not been defined and the boundary
between a marginal or ‘expanded’ donor, and a standard donor, remains the purview of individual programs (71). The question of the boundary between technical innovation/improvement and clinical research involving investigational review committees and separate informed consent is particularly relevant to SLT. In our view, the issue of SLT and donor selection should be addressed with the patient prospectively, when the patient is placed on the wait-list.

Discussion

Organ scarcity and increasing wait-list morbidity were the impetus for the development of SLT. Today, the discrepancy between organ supply and recipient demand has never been greater. This has renewed interest in increased application of traditional adult/pediatric SLT and performance of adult/adult SLT. A decade of experience with left lateral segment grafts has demonstrated that SLT applied to pediatric recipients yields excellent outcomes with significant decreases in pediatric wait-list times, wait-list morbidity, and lower utilization of living-donation at centers that routinely implement these techniques (27,29,74). Published comparisons between children receiving split and living donor left lateral segment grafts confirm comparable benefits from split liver grafts (27) (53). The benefits of SLT, without donor risk, make it our preferred technique for the transplantation of infants and small children without access to cadaver whole-organs.

Evolution of SLT is the product of Herculean efforts by a select group of centers around the world who have overcome significant barriers. Despite these efforts, SLT remains an infrequent procedure, principally applied in the setting of adult-pediatric pairs with at least one recipient being critically ill, that only a handful of U.S. transplant centers routinely perform. The authors assert that enhanced utilization and improved results will only be possible through improved information sharing, resolution of technical, logistic, and public policy issues, as well as liberalization of allocation criteria to provide transplant centers discretion in matching donors and recipients with respect to graft mass and severity of recipient medical status.

The greater than 90% response of transplant centers to the ASTS survey demonstrates keen interest in SLT. Clearly, the crisis in organ donation that currently exists is universal and has heightened awareness of potential avenues for increased donation. Despite this widespread interest, only 45% of responding centers reported any experience with SLT and two-thirds had performed a total of less than five procedures. Graft sharing between centers is infrequent: the ASTS survey reported a 5% incidence of graft sharing between five centers, Yersiz et al. have reported sharing three left lateral segment and 22 right trisegment grafts (27), Azoulay et al. has reported sharing four of 36 SLT grafts (56), and Rela et al. have shared three of 41 grafts obtained from ex vivo SLT (70). While a ‘learning curve’ was not assayed by the ASTS survey, it certainly exists as demonstrated in liver living-donation (50,75). The unequal distribution of experience, coupled with a required ‘learning curve’, forecast that greater information sharing must occur prior to SLT achieving a larger role in alleviating the current organ crisis. Improved information sharing could stimulate greater center graft sharing that would increase experience and decrease reluctance to accept additional SLT grafts for transplantation. The data presented herein are encouraging; however, the data are unverifiable with obvious gaps in organ accountability. The lack of an organized information sharing or education system underscores the need for a verifiable, data collection instrument, to provide information on SLT. This has not been successfully implemented despite widespread calls for its creation. Data from such a registry would be prerequisite for modification of current allocation criteria. Until this occurs, data on these procedures will be extremely limited and dissemination inefficient.

The fate of adults who receive trisegment grafts remains controversial. Two series examined adult right trisegment recipients by comparing SLT recipients with adults receiving cadaver whole-organs during the same time period (27) or via case-matched controls (29). In each study, 1-year patient survival was comparable between SLT right trisegment and whole-organ recipients. While excellent single-center data exists, the ASTS survey data and the UNOS Scientific Registry data demonstrate inferior outcomes when applied to adults in urgent need of liver transplantation. The ASTS report of 387 split-grafts is the largest collection of data to date, but is subject to the natural limitations of a survey that depends upon voluntary participation and self-reporting. Similarly, the SRTR’s failure to identify specific SLT grafts and to detail complications limits interpretation. This question is fundamental for the future of SLT, as comparable outcomes between right trisegment grafts and cadaver whole-organs in recipients across categories of urgency and indication is prerequisite for SLT to be further applicable and recognized in allocation policy.

References


